

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. (Previously presented) A method of treating a subject with a cancer, the method comprising administering to the subject an inhibitor of indoleamine-2,3-dioxygenase in an amount effective to reverse indoleamine-2,3-dioxygenase-mediated immunosuppression, and administering at least one additional therapeutic agent, wherein the administration of the inhibitor of indoleamine-2,3-dioxygenase and the at least one additional therapeutic agent demonstrate therapeutic synergy, wherein the at least one additional therapeutic agent is a cytotoxic antineoplastic chemotherapy agent, and wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan.
2. (Original) The method of claim 1, wherein the indoleamine-2,3-dioxygenase-mediated immunosuppression is mediated by an antigen presenting cell (APC).
3. (Cancelled)
4. (Previously presented) The method of claim 1, wherein the antineoplastic chemotherapeutic agent is selected from the group consisting of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, vincristine, ifosfamide, cisplatin, gemcytabine, busulfan, ara-C, and combinations thereof.
5. (Withdrawn) A method of treating a subject with a cancer, the method comprising administering to the subject an inhibitor of indoleamine-2,3-dioxygenase in an amount effective to reverse indoleamine-2,3-dioxygenase-mediated immunosuppression, and administering at least

one additional therapeutic agent, wherein the administration of the inhibitor of indoleamine-2,3-dioxygenase and the at least one additional therapeutic agent demonstrate therapeutic synergy, wherein at least one additional therapeutic agent is radiation therapy, and wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan.

6. (Withdrawn) The method of claim 5 wherein the radiation therapy is localized radiation therapy delivered to the tumor.

7. (Withdrawn) The method of claim 5 wherein the radiation therapy is total body irradiation.

8. (Cancelled)

9. (Original) The method of claim 1 wherein the inhibitor of indoleamine-2,3-dioxygenase is 1-methyl-tryptophan.

10. (Withdrawn) The method of claim 5 wherein the inhibitor of indoleamine-2,3-dioxygenase is 1-methyl-tryptophan.

11. (Previously presented) The method of claim 1 wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of the D isomer of 1-methyl-tryptophan, the D isomer of β -(3-benzofuranyl)-alanine, the D isomer β -(3-benzo(b)thienyl)-alanine, and the D isomer of 6-nitro-D-tryptophan.

12. (Withdrawn) The method of claim 5 wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of the D isomer of 1-methyl-tryptophan, the D

isomer of β -(3-benzofuranyl)-alanine, the D isomer of β -(3-benzo(b)thienyl)-alanine, and the D isomer of 6-nitro-D-tryptophan.

13. (Original) The method of claim 1, wherein the cancer is selected from the group consisting of melanoma, colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, leukemia, brain tumors, lymphoma, sarcoma, ovarian cancer, and Kaposi's sarcoma.

14-29 (Cancelled)

30. (Previously presented) The method of claim 1 further comprising administering a cytokine.

31. (Original) The method of claim 30 wherein the cytokine is granulocyte-macrophage colony stimulating factor (GM-CSF) or flt3-ligand.

32. (Previously presented) A method of augmenting the rejection of tumor cells in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one cytotoxic antineoplastic chemotherapeutic agent, wherein the rejection of tumor cells obtained by administering both the inhibitor of indoleamine-2,3-dioxygenase and the cytotoxic antineoplastic chemotherapeutic agent is greater than that obtained by administering either the inhibitor of indoleamine-2,3-dioxygenase or the cytotoxic antineoplastic chemotherapeutic agent alone.

33. (Previously presented) A method of treating cancer, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-

tryptophan and administering at least one cytotoxic antineoplastic chemotherapeutic agent, wherein the cancer survival rate observed by administering both the inhibitor of indoleamine-2,3-dioxygenase and the cytotoxic antineoplastic chemotherapeutic agent is greater than the cancer survival rate observed by administering either the inhibitor of indoleamine-2,3-dioxygenase or the cytotoxic antineoplastic chemotherapeutic agent alone.

34. (Previously presented) A method of reducing tumor size or slowing tumor growth in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one cytotoxic antineoplastic chemotherapeutic agent, wherein the tumor size or tumor growth observed with the administration of both the inhibitor of indoleamine-2,3-dioxygenase and the cytotoxic antineoplastic chemotherapeutic agent is less than the tumor size or tumor growth observed with the administration of either the inhibitor of indoleamine-2,3-dioxygenase or the cytotoxic antineoplastic chemotherapeutic agent alone.

35. (Withdrawn) A method augmenting rejection of tumor cells in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering radiation therapy, wherein the rejection of tumor cells wherein the rejection of tumor cells obtained by administering both the inhibitor of indoleamine-2,3-dioxygenase and the radiation therapy is greater than that obtained by administering either the inhibitor of indoleamine-2,3-dioxygenase or the radiation therapy alone.

36. (Withdrawn) A method of treating cancer, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan

and administering radiation therapy, wherein the cancer survival rate observed by administering both the inhibitor of indoleamine-2,3-dioxygenase and radiation therapy is greater than the cancer survival rate observed by administering either the inhibitor of indoleamine-2,3-dioxygenase or radiation therapy alone.

37. (Withdrawn) A method of reducing tumor size or tumor growth in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering radiation therapy, wherein the tumor size or tumor growth observed with the administration of both the inhibitor of indoleamine-2,3-dioxygenase and radiation therapy is less than the tumor size or tumor growth observed with the administration of either the inhibitor of indoleamine-2,3-dioxygenase or radiation therapy alone.

38. (Withdrawn) The method of claim 5, wherein the indoleamine-2,3-dioxygenase-mediated immunosuppression is mediated by an antigen presenting cell (APC).

39. (Withdrawn) The method of claim 5, wherein the cancer is selected from the group consisting of melanoma, colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, leukemia, brain tumors, lymphoma, sarcoma, ovarian cancer, and Kaposi's sarcoma.

40. (New) A method of treating a subject with cancer, the method comprising administering to the subject a pharmaceutical composition consisting essentially of 1-methyl-D-tryptophan.

41. (New) The method of claim 40, wherein the composition further comprises at least one cytotoxic antineoplastic chemotherapeutic agent, and wherein the administering of 1-methyl-D-tryptophan and the agent demonstrates therapeutic synergy.

42. (New) A method of treating a subject with cancer, the method comprising administering to the subject a pharmaceutical composition comprising 1-methyl-D-tryptophan, but not 1-methyl-(D,L)-tryptophan.
43. (New) The method of claim 42, wherein the composition comprises 1-methyl-D-tryptophan, but not 1-methyl-L-tryptophan.
44. (New) The method of claim 42, wherein the composition further comprises at least one cytotoxic antineoplastic chemotherapeutic agent, and wherein the administering of 1-methyl-D-tryptophan and the agent demonstrates therapeutic synergy.
45. (New) A method of reducing tumor size or slowing tumor growth in a subject, the method comprising administering to the subject a pharmaceutical composition consisting essentially of 1-methyl-D-tryptophan.
46. (New) The method of claim 45, wherein the composition further comprises at least one cytotoxic antineoplastic chemotherapeutic agent, and wherein the tumor size or tumor growth observed after administration of a pharmaceutical composition consisting essentially of 1-methyl-D-tryptophan and further comprising at least one cytotoxic antineoplastic chemotherapeutic agent is lower than the tumor size or tumor growth observed after administration of either a composition consisting essentially of 1-methyl-D-tryptophan alone or a composition comprising the cytotoxic chemotherapeutic agent alone.
47. (New) A method of reducing tumor size or slowing tumor growth in a subject, the method comprising administering to the subject a pharmaceutical composition comprising 1-methyl-D-tryptophan, but not 1-methyl-(D,L)-tryptophan.

48. (New) The method of claim 47, wherein the composition comprises 1-methyl-D-tryptophan, but not 1-methyl-L-tryptophan.
49. (New) The method of claim 47, wherein the composition further comprises at least one cytotoxic antineoplastic chemotherapeutic agent, and wherein the tumor size or tumor growth observed after administration of a pharmaceutical composition comprising 1-methyl-D-tryptophan, but not 1-methyl-(D,L)-tryptophan, and further comprising at least one cytotoxic antineoplastic chemotherapeutic agent is lower than the tumor size or tumor growth observed after administration of either a composition comprising 1-methyl-D-tryptophan, but not 1-methyl-(D,L)-tryptophan, or a composition comprising the cytotoxic chemotherapeutic agent alone.
50. (New) The method of claim 41, 44, 46, or 49, wherein the antineoplastic chemotherapeutic agent is selected from the group consisting of: cyclophosphamide, methotrexate, fluorouracil, doxorubicin, vincristine, ifosfamide, cisplatin, gemcytabine, busulfan, and ara-C.
51. (New) The method of claim 40 or 42, wherein the cancer is selected from the group consisting of melanoma, colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, leukemia, brain tumors, lymphoma, sarcoma, ovarian cancer, and Kaposi's sarcoma.
52. (New) The method of claim 45 or 47, wherein the tumor is a result of a cancer selected from the group consisting of melanoma, colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, leukemia, brain tumors, lymphoma, sarcoma, ovarian cancer, Kaposi's sarcoma, Hodgkin's Disease, multiple myeloma, neuroblastoma, stomach cancer, cervical cancer, endometrial cancer, testicular cancer, thyroid cancer, esophageal cancer, genitourinary tract cancer, premalignant skin lesions, and adrenal cortical cancer.

Supplemental Amendment

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For: USE OF INHIBITORS OF INDOLEAMINE-2,-DIOXYGENASE IN COMBINATION WITH OTHER
THERAPEUTIC MODALITIES

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53. (New) The method of claim 40, 42, 45, or 47, further comprising administering a cytokine.

54. (New) The method of claim 53, wherein the cytokine is granulocyte-macrophage colony stimulating factor (GM-CSF) or its flt3-ligand.

55. (New) The method of claim 40, 42, 45, or 47, wherein the composition further comprises a pharmaceutically acceptable carrier.

56. (New) The method of claim 40, 42, 45, or 47, wherein the composition is formulated for oral, rectal, nasal, topical, transdermal, aerosol, buccal, sublingual, vaginal, parenteral, subcutaneous, intramuscular, intravenous, intradermal, enteral, intraperitoneal, or intravesical administration.

57. (New) The method of claim 56, wherein the composition is formulated for oral delivery.

58. (New) The method of claim 57, wherein the composition is formulated in a tablet or capsule.

59. (New) The method of claim 58, wherein the composition is formulated for a controlled or sustained release.

60. (New) The method of claim 40, 42, 45, or 47, wherein the composition is formulated as an ointment, gel, solution, patch, or implant.

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61. (New) The method of claim 40, 42, 45, or 47, wherein the composition further comprises one or more diluents, buffers, binders, disintegrants, surface active agents, thickeners, lubricants, or preservatives.

62. (New) The method of claim 40, 42, 45, or 47, wherein the administering is carried out in a number of doses at intervals of time.

63. (New) The method of claim 40, 42, 45, or 47, wherein the composition is administered before, during, or after surgical resection, radiation therapy, chemotherapy, hormone therapy, anti-tumor vaccination, antibody-based therapy, cytokine-based therapy, whole body irradiation, bone marrow transplantation, and peripheral stem cell transplantation.